DOCKET NO.: ISIS-5315

Application No.: 10/698,689

Preliminary Amendment - First Action Not Yet Received

Amendments to the Specification:

Please insert the Sequence Listing being filed concurrently herewith into the specification.

Please replace paragraph 133 with the following.

For example, a duplex comprising an antisense strand having the sequence CGAGAGGCGGACCGG [SEQ ID No. 161] and having a two-nucleobase overhang of deoxythymidine(dT) would have the following structure:

Please replace paragraph 134 with the following.

In another embodiment, a duplex comprising an antisense strand having the same sequence CGAGAGGCGGACGGACCG may be prepared with blunt ends (no single stranded overhang) as shown:

cgagaggcggacgggaccg Antisense Strand [SEQ ID No. 161]

Please replace paragraph 142 with the following.

In accordance with the present invention, a series of antisense sequences were designed to target different regions of the human CD40 mRNA, using published sequences [Stamenkovic et al., *EMBO J.*, 8, 1403 (1989); GenBank accession number X60592, <u>SEQ ID No. 85</u>]. The sequences are shown in Table 1.

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Application No.: 10/698,689 Preliminary Amendment - First Action Not Yet Received Please amend Table 4, spanning pages 83-87 as follows.

Table 4 CD40 Antisense Sequence Alignment

06	TGCGGCTGCTTGCTGGGGCTGCTTGCTGGGGCTGCTTGC	180	TGTGCCAGCCAGAC TGTGCCAGCCAGGAC TGTGCCAGCCAGGA- TGTGCCAGCCAGGA- TGTGCCAGCCAGGA- TGTGCCAGCCAGGA- TGTGCCAGCCAGGAC
9/	TCTGG	166	TGTGCCAGO TGTGCCAGO TGTGCCAGO TGTG TGTG TGTGCCAGO
. 42	CTCTGCAGTGCGTCC	151 165	-TCAGTGCTGTTCTT
46 60	ATGGTTCGTCTGC	136 150	AGTACCTAATAAACA
31 45	BGTCTCACCT	121 135	CATGCAGAGAAAAC
30	TGGTCTGCG	106 120	AGAACCACCACTG AGAACCACCCACTG AGAACCACCACTG AGAACCACCACTG
1 15 16		91 105 106	TGTCCATC CAGAACCACCACTGTGTCCATC CAGAACCACCCACTGTGTCCATC CAGAACCACCCACTGTGTCCATC CAGAACCACCCACTG TGACCGCTGTCCATC CAGAACCACCTG TGACCGCTGTCCATC CAGAACCACTG TGACCGCTGTCCATC CAGAACCACCCACTG
SEQ ID NO:	[9] 173 [8] 172 [7] 171 [6] 170 [5] 169 [4] 168 [3] 167 [2] 166 [1] 165 x60592-CD40	;	(19) 183 (18) 182 (17) 181 (16) 180 (15) 179 (13) 177 (12) 176 (11) 175 (10) 174 (9) 173 (8) 173 (7) 171 (7) 171

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Table 4, continued

	CCTGGAACAGAGA	 CCTGGAACAGAGAGA	360	ACCATCTGCACCT ACACCATCTGCACCT ACACA
255 256			345 346	
25	TAGACA	GCGAATTCC TAGACA	34	CAGAAAC CAGAAAC CAG
240 241			330 331	
226 240	TTCCTTGCGGTGAA-	TTCCTTGCGGTGAAA	316 330	AGCAGAAGGGTCCAGCAGAAGG
225 2			315 3	
211	CTGAAACGGAATGCC CTGAAACGGAAT CTG	CTGAAACGGAATGCC		CCAACCTAGGGCTTC
196 210		cacagagttca	286 300 301	
195 1			285 2	
181		AGAGAAACTGGTGAG	271 2	CACACTGCCACCAGC
	[27] 191 [26] 190 [25] 189 [24] 188 [23] 187 [22] 186 [20] 185 [20] 184 [19] 183		5	[36] 200 [36] 200 [37] 199 [32] 198 [32] 196 [31] 195 [30] 194 [29] 193 [27] 193 [27] 193 [27] 193

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Table 4, continued

450	GATTG GGGTCAAGCAGATT-	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1								GGGTCAAGCAGATTG	540	GA	ACCCTTGGA	AATGTCACCCTTGGA	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1			1				CACCCTTGGA	
436	 GGGT(1		1 1	1	1 0).I.S GGGI	526		1	AATG	1			1	1		1	1	 	AATG	
435		GCTCGCCCGGCTT		1		1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1				ectescesectris	525		1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	AA	CATCTGCTTTCGA	CATCTGC			1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1			1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	 	CATCTGCTTTCGAAA AATGTCACCCTTGGA	
421		GCTC	1					-	C	5. 1.2.2.2.2.2.2.2.2.2.2.2.2.2.2.2.2.2.2.	511	1	`		CAIC	CAIC	CATC-			1			1	CATC	
420		CTCAT	TCCTGCACCGCTC	TCCTGCA						TCCTGCACCGCTCAT	510		1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		TSTST	CTCCAATGTGT	-CTTCTCCAATGTGT	TCTTCTCCAATG						TCTTCTCCAATGTGT	
406				-	TCC-	-	-	-			496	1	!		-	-	-CI		-	-	-	-	-		
391 405		1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	CIGIG	TGAGAGCIGIG	CCTGTGAGAGCTGTG					CCI'G TGAGAGCTGTG	481 495							TCGGCT	CCTGCCCAGTC	CCTGCCCA	CCTGC			CCTGCCCAGTCGGCT	
376 390)	ACTGTA				ACTGTACGAGTGAGG	480								TGCGAGC	ATCTGCGAGC	CCATCTGCGAGC	ATACCATCTGCGAGC .	ATAC	ccarccargc	
375 37						AAGAAGGCTGGC P	STGAAGAAGGCTGGC A	3TGAA		stgaagaaggciggc A	151 465 4						,			1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		CTG P	-TACAGGGTTTCTG P	CTACAGGGGTTTCTG ATA	
.,	[44] <u>208</u> - [43] <u>207</u> -	[42] 206	[41] 205	[40] 204	[39] 203	[38] 202	[37] 201	[36] 200		X60592-CD40 (220	219	218	217	216	215	214	213	212	211	210	[45] 209	208 92-CD40	

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Table 4, continued

630	AGAGCC AGAGCCC A			agagccc	720	ACCAAIA	 ACCAATA
616	CTGAGAGCC ATCGGCTGA			ATCGG CTG	705 706	AGAGCCAALA	 AGAAGCCA
01 615 616				crgregreeceage	691 705	TCAAAA	
586 600 601					9 069 929	TGCTGGTCTTTA T TGGTGCTGGT	
585		C AACAGGCAGGCACAA AC-		ACAGGCAGGCACAA A	661 675 6		
556 570 571			AAGACCTG	CAAGCTGTGAGACCA AAGACCTGGTTGTGC AACAGGCACAA ACAAGACTGATGTTG TCTGTGGTCCCCAGG ATCGGCTGAGAGCCC	099		 : TTCGGGATCC
541 555			TGTGAGACCA AAGACCTG - CAAGCTGTGAGACCA A CAAGCTGTG	CAAGCTGTGAGACCA	631 645		TGGTGGTGATCCC TGGTGGTG TGGTGGTGATCCCCA
	(65) <u>229</u> (64) <u>228</u> (63) <u>227</u> (62) <u>226</u> (61) <u>225</u>	[59] <u>223</u> [59] <u>223</u> [58] 222	221 220 219	218 92-CD40		[69] <u>233</u> [68] <u>232</u> [67] <u>231</u> [66] 230	

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Table 4, continued

810	CAGTGCAGGAGACTT CA	AGGAGACTT	006 1		GCACCCACCCAGGAG	976 846CTATGCCCAGTC		GAGCTATGCCCAGTC	
962	CAGTGC CAGTGC CAGT C C C C C C C C C C C C C C C C C C C	CAGTGC	886 GCACC-					GAGCTA	
781 795	CCAACACTGCTGCTC CCA	ACACTGCTG	871 AGACAGTGAGGCT GCACC AGAGACAG		 AGAGACAGTGAGGCT	961 975	GCAGGCAGAAG	GCAGGCAGAAGCGGG	
. 082 292			856 870 8 		GCATCTCAGTGCAGG	946 960	CAGGGGT (TGCTGCTGCAGGGGT (
751 765		AGATCAATTTTCCCG	841 855	ATGGCAAAGAG 	ATGGCAAAGAGAGTC	931 945		CAGAGAGCCTGGTGC	
736 750	AGCAGGAACCCG	AGGAACCCCAGG	826 840	CGCAGGAGG CG	CGGTCACCCAGGAGG	916 930		390	
721 735		CCCCCCACC	811 825	TACATGGATGCCAAC	TACTACATGCCAAC	901 915	1 C C C C C C C C C C C C C C C C C C C	TGTGGCCACGTGGGC	991 1004 AGTAGTGCCAGCCCTC
	(78) 242 (77) 241 (76) 240 (75) 239 (74) 238 (73) 237 (71) 235 (71) 235 (70) 234	X60592-CD40		[79] <u>243</u> [78] <u>242</u> [77] <u>241</u>		[841 248	[83] <u>247</u>	X60592-CD40	[84] <u>248</u> X60592-CD40

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Please replace paragraph 192 with the following.

Total RNA was isolated using an RNeasy Mini Kit (Qiagen). Two-step RT-PCR was performed using primers complementary to sequences of the CD40 gene (Genbank accession# M83312, incorporated herein as SEQ ID NO: 92). Reverse transcription was performed using a reverse primer (5'-TGATATAGAGAAACACCCCGAAAATGG-3'; SEQ ID NO: 93) complementary to sequence in exon 7. The resulting cDNA was subjected to 35 cycles of PCR using a forward primer consisting of a sequence span identical to that found in exon 5 of the gene (5'-GCCACTGAGACCACTGATACCGTCTGT-3'; SEQ ID NO: 94) as well as the reverse primer used for cDNA generation. The resulting PCR products were separated on a 1.6% agarose gel. PCR products were excised and the DNA purified. The resulting products were sequenced using primers used in PCR. Real-time quantitative RT-PCR was performed on total RNA from BCL1 or primary macrophages using an ABI Prism® 7700. Primer and dual labeled probe sequences were as follows:

Mouse IL-12 p40:

forward 5'-GCCAGTACACCTGCCACAAA- 3', SEQ ID No. 95

reverse 5'-GACCAAATTCCATTTTCCTTCTTG-3', SEQ ID No. 96

probe 5'-FAM-AGGCGAGACTCTGAGCCACTCACATCTG-TAMRA-3',

SEO ID No. 97

Mouse CD18:

Forward 5'-CTGCATGTCCGGAGGAAATT-3' SEQ ID No. 98

Reverse 5'-AGCCATCGTCTGTGGCAAA-3' SEQ ID No. [9] 99

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Probe 5'-FAM-CTGGCGCAATGTCACGAGGCTG-TAMRA-3', SEQ ID
No. 100

Mouse CD40, Type 1:

Forward 5'-CACTGATACCGTCTGTCATCCCT-3' SEQ ID No. 101

Reverse 5'-AGTTCTTATCCTCACAGCTTGTCCA-3' SEQ ID No. 102

Probe 5'-FAM-AGTCGGCTTCTTCTCCAATCAGTCACTT-TAMRA-3'

SEQ ID No. 103

Mouse CD40, Type 2:

Forward 5'-CACTGATACCGTCTGTCATCCCT-3' SEQ ID No. 104

Reverse 5'-CCACATCCGGGACTTTAAACCTTGT-3' SEQ ID No. 105

Probe 5'-FAM-CCAGTCGGCTTCTTCTCCAATCAGTCA-TAMRA-3' SEQ

ID No. 106

Mouse CD40:

Forward 5'-TGTGTTACGTGCAGTGACAAACAG-3' SEQ ID No. 107

Reverse 5'-GCTTCCTGGCTGGCACAA-3' SEQ ID No. 108

Probe 5'-FAM-CCTCCACGATCGCCAGTGCTGTG-TAMRA-3' SEQ ID

No. 109

Mouse cyclophilin:

Forward 5'-TCGCCGCTTGCTGCA-3' SEQ ID No. 110

Reverse 5'-ATCGGCCGTGATGTCGA-3' SEQ ID No. 111

Probe 5'-FAM-CCATGGTCAACCCCACCGTGTTC-TAMRA-3' SEQ ID

No. 112

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Please amend Table 9, spanning pages 112-121 with the following.

Table 9

Additional PNA Cationic Conjugate Compounds of SEQ ID NO: 124

Isis #-Lot#	N-terminal modification	C-terminal modification	notes	CD40 Protein (% UTC @ 10 µM)	t _{1/2} [h] in 25% mouse serum	Est. t _{1,2} [h] in 100% mouse serum
208529-1		K		80, 98, 100	stable	stable
278640-1	K	K		80	n.d.	
278641-1	K_2	K		06	n.d.	
278642-1	K ₃	K		80	n.d.	
278643-1	K ₄ (SEQ ID NO: 161)	K		100	n.d.	
278644-1	K ₅ (SEQ-ID-NO: 162)	K		70	n.d.	
278645-1	K ₆ (SEQ ID NO: 163)	K		50	n.d.	
278646-1	K ₇ (SEQ ID NO: 164)	K		30	n.d.	
278647-1	K ₈ (SEQ ID NO: 165)	K		20, 30, 35, 30, 15	5.7	1.4
287294-1	K ₈	K	4 mm	100	n.d.	
287293-1	K_6	K	4 mm	100	n.d.	
284381-1		K_2		95	n.d.	
279866-1		K4		85	6.5	1.6
284375-1		K ₈		40, 35, 35, 40, 35, 45, 73, 68	1	0.25
290075-1	R	К		100	n.d.	
290076-1	R ₂	K		96	n.d.	

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Isis #-Lot#	N-terminal modification	C-terminal modification	notes	CD40 Protein (% UTC @ 10 μM)	t ₁₂ [h] in 25% mouse serum	Est. t ₁₂ [h] in 100% mouse serum
290077-1	R ₃	K		06	n.d.	
290078-1	R4 (SEQ-ID-NO: 166)	K		08	n.d.	
290079-1	R ₅ (SEQ ID NO: 167)	K		08	n.d.	
297780-1	R ₆ (SEQ-ID NO: 168)	K		75	n.d.	
290081-1	R, (SEQ ID NO: 169)	K		02	n.d.	
290082-2	R ₈ (SEQ-ID NO: 170)	K		09	3.2	8.0
301010-1	D-R ₈	K		49	n.d.	
299870-1		K ₅ RK ₂ (SEQ ID NO: 171)		48	n.d.	
299871-1		D(K ₅ RK ₂) (SEQ ID NO: 172)		53	n.d.	
284382-1	K_2	K_2		85	n.d.	
279867-1	K ₄	K4		75	n.d.	
284383-1	Ada-O	K_2		80	n.d.	
284384-1	Ada-O-K ₂	K_2		85	n.d.	
279975-1	Ada-O	K4		95	n.d.	
279976-1	Ada-O-K4	K4		75	n.d.	
284376-1	Ada-O	K_8		40	n.d.	
284385-1	Pam-O	K_2		n/a tox.	n.d.	
284386-1	Pam-O-K ₂	K_2		n/a tox.	n.d.	
283582-1	Pam-O	K4		70	n.d.	
283583-1	Pam-O-K4	K4		09	n.d.	

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Isis #-Lot#	N-terminal modification	C-terminal modification	notes	CD40 Protein (% UTC @ 10 µМ)	t ₁₂ [h] in 25% mouse serum	Est. t ₁₂ [h] in 100% mouse serum
284377-1	Pam-O	K ₈		n/a tox.	n.d.	
290061-1	O-nqI	K ₂		80	n.d.	
287086-1	O-nqI	K_8		30	1	0.25
311573-1	Ibu-O-K ₈	К		n.d.	n.d.	
290063-1	СНА-0	K_2		95	n.d.	
290064-1	Chol-O-	K_2		n/a tox.	n.d.	
292097-1	CHA-O-K ₈	K		55	n.d.	
292098-1	Chol-O-K ₈	K		n/a tox.	n.d.	
298110-1	Branch1-K	K		09	n.d.	
298111-1	Branch3-K	K		85	n.d.	
298112-1	Branch4-K	K		09	n.d.	
298113-1	Branch5-K	K		75	n.d.	
298114-1	Branch6-K	K		70	n.d.	
298116-1	Branch2-K	У		40	n.d.	
303537-1	RacaRRacaRR	K		23, 29	2	0.5
303540-1	KacaKKacaKKacaKK	К		70	n.d.	
303538-1	RacaRacaRacaRac aRacaR	K		40	n.d.	
309743-1	dR.aca.dR.dR.aca.dR.d R.aca.dR.dR	K		35	n.d.	
303539-1	KacaKacaKacaKac aKacaK	K		61	n.d.	į

Isis #-Lot#	N-terminal modification	C-terminal modification	notes	CD40 Protein (% UTC @ 10 µM)	t _{1.7} [h] in 25% mouse serum	Est. t ₁₂ [h] in 100% mouse serum
291341-1	KGKKGKGK (SEQ ID NO:-173)	K		87	n.d.	
291342-1	KaocKKaocKaocK	K		79	n.d.	
330890-1	hR-O-hR-hR-O-hR-hR- O-hR-hR	К		25 at 3 uM	59	12
338896-1	hR-O-R-hR-O-R-hR-O- R-hR	К		49	2	0.5
338897-1	R-O-hR-R-O-hR-R-O- hR-R	K		54	4	1
315570-1	RacaRRacaRRacaRR- PKKKRKV	K		25	n.d.	
315571-1	RacaRRacaRRacaRR- KKVKPKR	K		41	n.d.	
315650-1	PKKKRKV- RacaRRacaRR	K		44	n.d.	
315573-1	KKVKPKŘ- RacaRRacaRRacaRR	K		31	n.d.	
309860-1	R-βA-RR-βA-RRβA- RR	K		27	n.d.	
309883-1	R-abu-RR-abu-RR-abu- RR	K		26	n.d.	
309861-1	R-aoc-RR-aoc-RR-aoc- RR	K		25	n.d.	
309864-1	R-aca-RR-aca-RR-aca- RR-aca	K		20	n.d.	
309862-1	R-O-RR-O-RR-O-RR	K		24	2	0.5

RR-aca-RR-aca-RR K-aca-RR-RR-aca-RR-RR-RR-RR-RR-RR-RR-RR-RR-RR-RR-RR-RR	modification	(% UTC @ 10 μM)	mouse serum	100% mouse serum
	K	40	n.d.	
	K	88	n.d.	
R-inp-RR-inp-RR-inp-	Σ	29	n.d.	
R-amc-RR-amc-RR- Kamc-RR	Y	27	n.d.	
(BK) ₈	K	99	n.d.	
BK-BK-KKKK-BK-BK K	K	52	n.d.	
(K-BK) ₄	K	62	n.d.	
KK-0K-KK-0K-KK	>	19	n.d.	
D-(Om) ₈	K	<i>L</i> 9	n.d.	
)	(Om) ₈	64	n.d.	
(Om) ₈	K	LL	> 48	> 12
Om-Om-KKKK-Om- k Om	K	52	n.d.	
(K-Om) ₄	K	42	n.d.	
KK-Om-KK-Om-KK	K	34	19	4.75
KKKKK-Om-KK	K	95	n.d.	
KK-Om-KKKKK	K	53	n.d.	
(dK) ₈	K	54	stable	> 48
dKdK-KKKK-dKdK	K	09	n.d.	
K-dK-K-dK-K-dK-K- dK	К	69	n.d.	

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	modification	modification	notes	СD40 Protein (% UTC @ 10 µM)	t _{i,2} [h] in 25% mouse serum	Est. t _{1/2} [n] in 100% mouse serum
305392-1 I	KK-dK-KK-dK-KK	Ж		62	stable	> 48
311071-1	KKKKK-dK-KK	К		61	n.d.	
311072-1 F	KK-dK-KKKKK	K		59	n.d.	
305393-1 I	RRKKKKRR (SEQ ID NO: 174)	К		65	n.d.	
305394-1 F	KRKRKRKR (SEQ ID NO: 175)	К		52	n.d.	
305395-1 F	KKRKKRKK (SEQ-ID NO:176)	У		. 43	2.5	9.0
308579-1	(hK) ₈	K		31	18	4.5
308580-1	һКһК-КККК-һКһК	Х		34	n.d.	
308581-1 F	K-hK-K-hK-K-hK-K- hK	К		32	n.d.	
308582-1 F	KK-hK-KK-hK-KK	K		31	7.5	1.9
316409-1	(Dab) ₈	Х		77	> 48	> 12
316410-1 ((Dab) ₂ -K-(Dab) ₂ -K- (Dab) ₂	K		64	n.d.	
316411-1	(Dab-K)4	К		/ 52	n.d.	
316412-1 I	KK-Dab-KK-Dab-KK	K		38	40	10
316427-1	(K-ab) ₈	K		47	n.d.	
316428-1	(K-(K-ab))4	К		41	n.d.	
316429-1 I	KK-(K-ab)-KK-(K-ab)- KK	K		39	n.d.	

Isis #-Lot#	N-terminal modification	C-terminal modification	notes	CD40 Protein (% UTC @ 10 µM)	t _{1,2} [h] in 25% mouse serum	Est. $t_{1/2}$ [h] in 100% mouse serum
316430-1	(K-ab) ₂ -K-(K-ab) ₂ -K- (K-ab) ₂	×		55	n.d.	
325598-1	(dmK) ₈	K		71	stable	
325599-1	(K-dmK)4	K		53	n.d.	
325600-1	KK-dmK-KK-dmK-KK	K		41	23	5.8
325601-1	(dmK) ₂ -K-(dmK) ₂ -K- (dmK) ₂	Ж		63	n.d.	
326744-1	(hR) ₈	K		30, 20	15.4	3.9
	(hhR) ₈	K		n/a	stable	stable
333677-1	(K-hR) ₄	K		44	n.d.	
333678-1	KK-hR-KK-hR-KK	К		36	n.d.	
338894-1	(DhR) ₈	K		n/a tox.	n.d.	
338895-1	RR-DhR-RR-DhR-RR	K		<i>L</i> 9	23.6	5.9
326746-1	(norR) ₈	K		90 at 3 uM	> 48	> 12
333674-1	G(pK) ₈	K		56	> 48	> 12
333675-1	(K-pK)4	K		70	n.d.	
333676-1	KK-pK-KK-pK-KK	K		09	29	7.25
332593-1	(H) ₈ (SEQ ID NO: 177)	К		64	44.5	11
332672-1	(KH) ₄ (SEQ ID NO:178)	K		73	n.d.	
332673-1	KKHKKHKK (SEQ ID NO: 179)	K		52	5.7	1.4
332674-1	KKGKKGKK (SEQ ID	К		59	n.d.	

Isis #-Lot#	N-terminal modification	C-terminal modification	notes	CD40 Protein (% UTC @ 10 µM)	t _{1.7} [h] in 25% mouse serum	Est. t _{1/2} [h] in 100% mouse serum
	NO: 180)					
313685-1	K ₇ -Ci	К		99	n.d.	
313686-1	K ₆ -Ci-K	K		59	n.d.	
313687-1	K ₅ -Ci-K ₂	К		53	n.d.	
313688-1	K4-Ci-K3	Х		52	n.d.	
313689-1	K ₃ -C-K ₄	У		57	n.d.	
313690-1	K ₂ -Ci-K ₅	Ж		. 55	n.d.	
313691-1	K-Ci-K ₆	К		57	n.d.	
313692-1	Ci-K ₇	K		52	n.d.	
313693-1	KK-Ci-KK-Ci-KK	K		65, 67	n.d.	
310755-1	K ₈ -βA	K		43	. n.d.	
310756-1	K ₈ -aca	K		48	n.d.	
310757-1	K ₈ -aoc	K		54	n.d.	
310758-1	K ₈ -adc	K		89	n.d.	
291335-2	K ₈ -aoc-aoc	K		62	n.d.	
310753-1	K ₈ -0	K		44	n.d.	
310754-1	K ₈ -0-0	Ж		46	n.d.	
330775-1	(dK) ₈ -FRGO	Ж		46	2.8	0.7
330776-1	(dK) ₈ -dF-dRGO	K		54	n.d.	
330777-1	(dK) ₈ -ALALGO	K		37	8.7	2.2
330778-1	(dK) ₈ -dA-dLdAdLGO	K		36	n.d.	

DOCKET NO.: ISIS-5315

Application No.: 10/698,689

Preliminary Amendment - First Action Not Yet Received

Isis #-Lot#	Isis #-Lot# N-terminal modification	C-terminal modification	notes	CD40 Protein (% UTC @ 10 µM)	t _{1/2} [h] in 25% mouse serum	Est. t ₁₂ [h] in 100% mouse serum	
335296-1	335296-1 (dK) ₈ -WEHDLO	К		59	> 48	. 12	
335299-1	335299-1 (dK) ₈ -dW-dE-dH-dD- dL-O	К		64	n.d.		
335297-1	335297-1 (dK) ₈ -D-E-V-D-L-O	K		06	> 48	> 12	
335300-1	335300-1 (dK) ₈ -dD-dE-dV-dD- dL-O	K		68	n.d.		
330781-1	330781-1 (dK) ₈ -G-F-L-G-O	K		38	> 48	> 12	
330782-1	330782-1 (dK) ₈ -G-dF-dL-G-O	K		39	n.d.		
339746-1	339746-1 dK ₈ -Cys-disulfide-Cys-O	K		41	17	4.25	
339747-1	339747-1 dK ₈ -Cys-disulfide-Pen-O	K		35	30	7.5	